the original Mulago Hospital gradually extended by the building of more huts until a hospital of 700 beds sprawled over the upper slope of Mulago Hill. In 1955, seeing the need for more modern, better facilities the Protectorate government sent the medical superintendent and an architect on a tour of hospitals in Africa and Europe to get ideas for the building of a new teaching hospital. The actual construction of the present beautiful 900-bedded hospital was carried through with remarkable expedition—from the first architect's sketch to completion took less than five years. It was opened by H.R.H. the Duchess of Kent in October 1962. The cost of the hospital amounted to £2,300,000, of which three-quarters was provided by the British government.

Degrees and Research

In 1963 the University of East Africa was founded, Makerere College becoming Makerere University College with two sister institutions at Nairobi and Dar-es-Salaam. The next year, at a colourful ceremony presided over by the Chancellor of the University, degrees in medicine of the University of East Africa were conferred on 30 new graduates and on 129 holders of the old L.M.S. (E.A.). The following year six graduates registered to take higher degrees in the faculty of medicine. Today almost 100 students graduate in medicine every year.

In 1965 Dr. J. S. W. Lutwama, a senior lecturer in the Department of Preventive Medicine, was promoted to be professor in that department. This appointment was of significance in that Dr. Lutwama was the first Makerere medical graduate to be appointed to a chair in his own school. A few months later, on the resignation of Professor D. Allbrook, Professor Lutwama was appointed Dean of the medical faculty.

The latter half of the 1960s were years of bustling activity and progress in many directions in the medical faculty. The undergraduate curriculum was constantly under review with the faculty anxious to experiment and make modifications in the light of experience. The planning of a new higher qualification, the Mastership in Medicine, which it was hoped would provide a training more relevant to the conditions in East Africa and make less necessary prolonged visits to

the U.K. to take the M.R.C.P., F.R.C.S., and other British higher qualifications, went ahead.

Research work expanded in many directions, grants to the medical school from foundations outside East Africa amounting to nearly half a million pounds in 1964-5. Particular efforts were made to encourage research work by Makerere students. An appeal to various commercial organizations in East Africa raised £2,000 as a fund for medical student research scholarships. In 1957 the first Makerere Medical students journal was launched with its primary aim "to act as a medium for the students to publish their first papers and through this to learn the discipline of devotion to the progress of medicine." Ten years later the journal had a circulation of over 1,000 and many interesting papers had been published in it.

The energy of some of the early postwar faculty members, particularly Professor J. N. P. Davies, had built up, with amazing rapidity, a really fine medical library—which was named after that pioneer of medical education in Uganda, Sir Albert Cook, many of whose own books have found a resting place there. In 1965 a gift of £27,000 from the Nuffield Foundation allowed the building of a substantial extension to the library.

As the decade wore on the turn-over of expatriate staff in the medical school steadily increased. After 1963 no expatriates were appointed to chairs on permanent terms, contracts of up to six years being offered instead. Despite political pressure to "Africanize" as rapidly as possible, the senior Ugandan members of the college were as unwilling as anyone to see unsuitable men appointed to chairs merely because they were Ugandans. Suitable Ugandans, however, were undergoing training and enlarging their experience either abroad or in East Africa and soon three more native Ugandans had joined Professor Lutwama in professorial rank.

This year is perhaps not the happiest time for Makerere Medical School's fiftieth anniversary to fall; the recent political upheavals in Uganda have greatly affected the institution and have led to the closure of units and the dispersal of staff, both native and expatriate. All who know Makerere, however, must be confident that this time of troubles will pass and the university and its medical school will take its rightful place as one of the premier institutions of medical science in the tropical world.

Hospital Topics

In Vivo Tests of Thyroid Function

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Despite the increasing emphasis on in vitro tests of thyroid function, in vivo tests are still widely used. The major applications of in vivo techniques are in the diagnosis of thyrotoxicosis and in the assessment of the functional activity of thyroid nodules by scanning the gland. The application of in vivo tests to the

diagnosis of hypothyroidism is limited. Technetium-99m is now being used to determine thyroid uptake because of its low energy and short half-life and because the isotope is not organically bound to tyrosine—though it is concentrated in the thyroid gland in the same way as iodine. In vivo tests may be subdivided into: (1) thyroid uptakes, (2) suppression tests, (3) stimulation tests, and (4) scans.

Thyroid Uptake

For nearly 20 years the uptake of ^{131}I by the thyroid gland has been used as a routine test of thyroid function. In general the

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rate of trapping of iodide by the thyroid gland reflects the rate of secretion of thyroid hormone into the circulation. Therefore in thyrotoxicosis the uptake of iodine by the thyroid gland is increased. The patient is given a tracer dose of ^{131}I of between 10-50 μCi by mouth and after a specified time (which usually varies between 10 minutes and 48 hours) the amount of ^{131}I in the neck is measured with a suitable radiation-detecting system. This value is then compared with that obtained by measuring an aliquot of the original dose in similar conditions and the result expressed as a percentage of the dose administered.

In hyperthyroidism both the proportion of the tracer dose accumulated by the gland and the rate at which this takes place are increased. The enhanced rate of accumulation is more appreciable in the early phase than it is 24 hours after administration. It is therefore advantageous to measure the early uptake by the gland and the time usually selected varies from 10 minutes to two hours. Ideally the uptake should be measured before any appreciable discharge of radioactivity from the gland as labelled hormone has occurred. Though the information obtained by the early uptake is more significant physiologically the physical measurement is technically more difficult. Early uptake measurements are of little help in the diagnosis of hypothyroidism.

Theoretically one of the problems of neck uptake measurement is to differentiate between the radioactivity coming from the thyroid gland itself and that coming from the blood traversing other tissues in the neck.

Corrections should therefore be made for extrathyroidal activity. Nevertheless, when an early iodine uptake is used these corrections are not necessary, for it has been shown that the uncorrected 30-minute ^{131}I uptake is diagnostically as efficient for differentiating between the hyperthyroid and the euthyroid patient as a corrected measurement, provided that due allowance is made for the change in the normal range.¹ Another advantage of the early uptake measurement is that there is no need for patients to return to hospital the next day; this is obviously necessary when the 24-hour uptake is used.

There are other disadvantages of a 24-hour uptake. The uptake measurement does not take into account the amount of radioactivity discharged from the gland as labelled hormone and this may be appreciable after six hours. Also the clearance of iodide by the kidneys influences the amount concentrated in the gland and this effect is more definite at 24 hours than at two hours.² If a 24-hour uptake is selected an additional measurement at two or four hours is necessary.

The amount of radioactive iodine taken up by the gland will be influenced by the amount of inorganic iodide in the serum. If the body store of iodide is low and the serum level of inorganic iodide reduced, the uptake of ^{131}I will be raised, though the total amount of iodide entering the gland may be normal. When stores of iodide are low most of the iodide derived from peripheral degradation of thyroxine is re-used. The thyroid hypertrophies to maintain a normal output of hormone by trapping a greater proportion of the circulating iodide from the blood. This gives rise to the hyperplastic non-toxic goitre of iodine deficiency. A high radioactive iodine uptake in a patient with a simple goitre of iodine deficiency may thus give rise to an erroneous diagnosis of toxic goitre. Conversely if the inorganic iodide stores of the body are increased owing to contamination there will be a decrease in the uptake of ^{131}I . Iodine is a constituent of health foods such as kelp, and of many cough mixtures. Organic iodide is a constituent of compounds used as radiographic contrast media. Iodine contamination has already been considered with reference to its effects on some of the *in vitro* tests of thyroid function.³

The ^{131}I uptake should not be used in children or during pregnancy because of the relatively high whole body radiation dose. If an uptake is required in these circumstances an isotope with a shorter half-life and lower energy such as ^{123}I or $^{99\text{m}}\text{Tc}$ should be used.

PB ^{131}I

The PB ^{131}I is a test which was widely used and is now rarely performed. It measures the amount of ^{131}I which has been incorporated into thyroid hormone and released into the circulation in a specified time. It is not a measure of serum thyroxine concentration. The measurement is best carried out at 48 hours, by which time nearly all the ^{131}I is protein-bound in the euthyroid patient. It depends not only on the rate of secretion of thyroid hormones but on the size of the iodine pool within the thyroid. In hyperthyroidism the size of the iodine pool is usually normal and a raised PB ^{131}I reflects an increased hormonal secretion rate. If, however, the thyroid iodine pool is reduced, a raised PB ^{131}I may mean no more than a reduced thyroidal iodine pool. This will happen if the patient has had a previous thyroidectomy; if much of the thyroid has been destroyed by ^{131}I therapy; or if the patient has lymphocytic destruction of part of the gland, as occurs in chronic thyroiditis. Moreover, if the amount of stored thyroxine is reduced radioactive hormone will be present in greater concentration and the same hormone output will contain more radioactive protein-bound iodine. Thus at times this test may be misleading in patients who have been treated with ^{131}I or by surgery, and also in children. There is little application for the test now as more reliable *in vitro* tests of thyroid function have become available which do not require the administration of radioactive material to the patient.

T-3 Suppression Test

The tri-iodothyronine (T-3) suppression test is useful in differentiating thyrotoxicosis from other causes of raised uptakes such as iodine deficiency, and in studying the autonomy of thyroid nodules. It may also help in the diagnosis of the patient with suspected hyperthyroidism in whom the uptake test is equivocal. Failure of suppression is characteristic of thyrotoxicosis.⁴ It is also common in patients with ophthalmic Graves's disease, when this may be the only abnormality of thyroid function.⁵

The test procedure is simple but there is a potential risk of inducing transient hyperthyroidism in patients who do not show suppression and this may be dangerous in elderly patients or those with heart failure. The initial uptake is measured and 120 μg of T-3 is then given daily by mouth for five days, after which the uptake is repeated. T-3 is used in preference to T-4 because of its more rapid effect and its shorter biological half-life. In normal people the thyroid uptake is suppressed by this amount of exogenous hormone. In thyrotoxicosis little or no suppression occurs. Patients with non-toxic goitre who have a high uptake show on average a fall of about 80%.⁶ Suppression is usually considered significant for a 24-hour uptake when the control value is reduced by more than half. The TRH test⁸ gives similar information and is likely to replace this investigation in centres where the radioimmunoassay of serum TSH is available.⁷

A modification of the T-3 suppression test has been used as an indicator of remission of disease in patients who are on anti-thyroid drug treatment for thyrotoxicosis.⁸ A return to normal suppressibility in treated patients might indicate a remission but as a test of remission it is not sufficiently reliable. Some patients who show suppression later relapse if antithyroid drugs are stopped, and some who do not show suppression remain in remission for several years.⁹ If technetium is used to measure uptake during treatment with an antithyroid drug, the difficulties of interpretation that occur when ^{131}I is used are avoided.¹⁰

TSH Stimulation Test

The TSH stimulation test was introduced to distinguish between primary and secondary hypothyroidism. An injection of TSH will cause a rise in uptake in patients with hypopituitarism but no rise takes place in patients with primary thyroid failure. To

differentiate between these two disorders uptakes are measured before and 24 hours after an injection of 10 IU of bovine TSH. A significant response is usually taken to be a doubling of the control value or an increase of 15%, whichever is greater.¹¹

This test may be used for assessing thyroid function without discontinuing treatment in patients who are being maintained on thyroid hormone. Such people have an immeasurable uptake whether or not they are hypothyroid, but if this is due to suppression of normal tissue by exogenous hormone then the uptake will rise if the gland is stimulated by TSH. In this way it is possible to decide whether patients on thyroid hormones were initially hypothyroid and do still require replacement therapy.

Information similar to that obtained from both the T-3 suppression test and the TSH stimulation test may be obtained by measuring serum TSH levels before and after an injection of the hypothalamic releasing hormone TRH.^{7,12} As radio-immunoassays of TSH are undertaken by more laboratories and as TRH becomes widely available probably the TRH test will supersede both the T-3 suppression and the TSH stimulation tests.

Other Isotopes Used

¹³¹I has been used for thyroid uptakes since 1954. A few centres prefer to use this isotope to ¹³¹I for routine diagnosis.¹³ Its principal advantages over ¹³¹I are the short half-life of 2.3 hours and a much lower radiation dose. It is thus suitable for use in children and in pregnant women and also when serial tests are required in the same patient. Measurements with this isotope are usually made four hours after an oral dose of 15 μ Ci. This interval is too long for this test to have the advantage of being an "early" uptake.

The most recent isotope to be used for neck uptakes is ^{99m}Tc which has a half-life of 6 hours. This isotope is concentrated in the thyroid gland but does not become organically bound to tyrosine. Its gamma ray energy is lower than both ¹³¹I and ¹³²I so the radiation dose to the thyroid from a tracer dose of ^{99m}Tc is about one ten-thousandth of that from ¹³¹I. The ^{99m}Tc uptake in a normal gland is low, about 2% of the administered dose, and so the neck background is high. An accurate correction for this must therefore be made in the calculation of the uptake. Scanning techniques are usually employed to measure this uptake to ensure that an accurate determination of the extra-thyroidal activity can be made. An early uptake is usually measured 20 minutes after an intravenous injection of 250-500 μ Ci of the isotope. This has the added advantage that the diagnosis can be made at the patient's first visit to the clinic. As the normal range is low this test has no application to the diagnosis of hypothyroidism. It may be used instead of ¹³¹I for both T-3 suppression tests and TSH stimulation tests.

Thyroid Scans

Thyroid scans were initially obtained by manually moving a detector over the gland and recording the concentrations at 1-cm intervals. Isocount curves were then drawn to delineate regions of high and low activity. Automatic scanning machines are now widely available and are used to obtain more information on the size, shape, and position of the gland and the topographical distribution of the tracer isotope. The procedure takes about 10 minutes. Both ¹³¹I and ^{99m}Tc are used: the ¹³¹I scan is normally obtained at 24 hours and the ^{99m}Tc scan is obtained at about half an hour.

As with many diagnostic procedures, thyroid scanning is not as rewarding as was once hoped. It is not necessary to scan all enlarged glands but it is helpful to scan the thyroid when a solitary nodule is palpated and in cases of suspected retrosternal goitre or ectopic thyroid tissue. The scan will distinguish between functioning and non-functioning thyroid nodules. A

single non-functioning thyroid nodule (fig. 1) should be removed as only histological examination can establish whether it is a carcinoma or whether it is one of the other causes of non-functioning nodules—such as an adenoma, a cyst, or a focal area of autoimmune thyroiditis. In only about half of the patients who appear to have single nodules on clinical examination is this confirmed at operation: the remainder have multiple nodules.¹⁴

FIG. 1—¹³¹I scan of a large non-functioning nodule in the lower part of the right lobe of the thyroid gland.

A functioning nodule is unlikely to be a carcinoma. If it is autonomous the isotope will all be concentrated within the nodule. Such nodules are likely to become toxic and produce hyperthyroidism (fig. 2).

FIG. 2—⁹⁹Tcm scan of an autonomous nodule which occupies the whole of the left lobe of the thyroid gland. The right lobe of the gland is suppressed and has not therefore concentrated any activity.

Conclusion

In vivo tests of thyroid function receive less emphasis today with the advent of more reliable in vitro tests which do not require the administration of radioactive isotopes to the patient. Nevertheless, the kinetic information provided by in vivo tests offers a particular advantage and the speed with which the result is available enables the clinical diagnosis to be confirmed at the patient's first attendance at the clinic.

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Any Questions?

We publish below a selection of questions and answers of general interest

B.C.G. for Asthmatics

Is it safe to give B.C.G. to asthmatic patients? Should any precautions be taken?

It is safe to give B.C.G. to asthmatic patients and they are unlikely to have any more complications than other people. Even children who have been on continuous small doses of prednisolone for several years have had no unusual reactions to B.C.G. vaccination. There is, however, a theoretical risk that large doses of steroid treatment might depress immune mechanisms and lead to disseminated B.C.G. infection. I have not seen this reported but unless the need for B.C.G. were particularly urgent it might be wise to defer its use in such cases.

Smith, J. M., *Tubercle*, 1963, 44, 281.

E.S.R. and Menstruation

Does the erythrocyte sedimentation rate vary throughout the menstrual cycle of a healthy woman?

The E.S.R. changes vary little during the menstrual cycle and these changes are not of clinical significance. The E.S.R. has a very subtle physico-chemical background, not often realized by the clinician searching for simple signposts, and results vary according to the method of estimation. The rate is more variable in women than in men and tends to be slightly higher in women, a difference not apparently due to hormone changes in the menstrual cycle. One method gives figures of 2 to 5 mm per hour for men and 3 to 8 mm per hour for women.¹

¹ Documenta Geigy, *Scientific Tables*, 7th edn., p. 558. Macclesfield, Geigy (U.K.) Pharmaceuticals, 1970.

Hazards of Prophylactic Penicillin

What are the hazards of giving penicillin prophylactically over several years to a child diagnosed as having had rheumatic fever?

I should put first the hazard that the child will not continue to take it regularly or in adequate doses. As a result, repeated beta-haemolytic streptococcal infections (which may be asymptomatic) are likely to occur, with possible recurrences of rheumatic fever and permanent damage to the heart. It is disappointing to find that parents may not understand this—perhaps because they are not told so repeatedly and every time the prescription is renewed. Adequate dosage of oral penicillin V (phenoxymethyl penicillin) means not one but two doses daily (125 mg b.d., half an hour before meals). A hazard of the prophylactically even more effective intramuscular benzathine

penicillin G (1,200,000 units once a month) is pain at the site of injection, persisting for two or three days, so the patient may be frightened to come back. Beta-haemolytic streptococci are loyal: they remain sensitive. When the patient is on penicillin other organisms—for example, candida, coliforms, or staphylococci—may flourish and cause stomatitis. If the patient who is on prophylactic penicillin needs dental treatment he should be given another antibiotic such as erythromycin a few hours before the treatment and for two days afterwards against the risk of penicillin-resistant *Streptococcus viridans* causing endocarditis.

A common hazard is the development of allergy, leading to rashes and anaphylaxis. Allergy is probably diagnosed too often but if it is suspected the child should be investigated at a dermatology clinic. A rare association between Stevens-Johnson syndrome and penicillin, as well as other antibacterials such as sulphonamides, has been noted. The hazards of penicillin or any other prophylactic drug therapy are real, but more dangerous to the patient could be the recurrences of rheumatic fever which penicillin can usually prevent.

Vitamin Supplements in Fat-free Diet

Should patients on a fat-free diet be given vitamin supplements?

A fat-free diet will obviously be lacking in the vitamins that normally accompany dietary fat. It is unlikely, however, that any tolerated human diet is entirely fat-free. Nevertheless, it would be sensible to supplement a diet low in fat with vitamins A, D, K, and E, and perhaps with the essential fatty acid linoleic acid.

Mixing Chlorpromazine and Morphine

Why does a precipitate form when chlorpromazine and morphine are mixed in a syringe? Is the mixture safe to use for injection?

According to Martindale¹ chlorpromazine is compatible with morphine hydrochloride 1%. The manufacturers (May & Baker Ltd.) say they have had no reports of incompatibility of chlorpromazine with morphine injection. Chlorpromazine is precipitated by alkalis and would be precipitated if the syringe was alkaline. Solutions of morphine salts are usually acidic. The B.P. injections of morphine sulphate and chlorpromazine both contain the antioxidant sodium metabisulphite, which usually renders solutions acidic. It is, of course, inadvisable to inject solutions containing a precipitate.

¹ Martindale, *The Extra Pharmacopoeia*, 26th edn., p. 1812. London, Pharmaceutical Press, 1972.